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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,631	01/28/2004	Zhong Zhang	TPIP018X2	3752

23122 7590 09/12/2007

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
09/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,631	ZHANG ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,12,20,23-37,39-64,66-68 and 71-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11,12,20,23-37,39-64,66-68 and 71-78* is/are rejected.

7)☒ Claim(s) *66, 71-72, 75 and 77* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/14/07;1/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

The response filed **01/08/07** presents remarks and arguments to the office action mailed **10/19/07**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of claims

Claims 1, 11-12, 20, 23-37, 39-64 and 71-78 are pending.

Claims13-19, 21, 23, 65 and 70 are cancelled.

Claims 1, 11-12, 20, 23-24, 26, 29-31, 33, 36-37, 39-57, 59, 63-64, 66, 71-72, 75, 77-78 are amended.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5/14/07 is received and acknowledged.

The information disclosure statement filed fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the year of publication is missing. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

Claims 66,71-72, 75 and 77 are objected to because of the following informalities: they contain improper periods therein. See, for example claim 66, line 3, which contains an improper period in "a.". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-25, 49-64, 66-68, 72 and 78 are/remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "less than about" and "between about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, because one of skill will not be able to determine which term is in control.
The term "from about", is not defined by the required claim 78, the specification does not provide a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, because one of skill will not be able to determine which term is in control. The claims lack clarity as to whether "from" (a lower limit) or "about"(broadening limitation, both higher and lower) controls the metes and bounds of the phrase "from about.

Claims 1-2, 11-12, 20, 23-37, 39-48 and 62-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required

feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "a block copolymer" and the claim also recites "namely poloxamer 188" which is the narrower statement of the range/limitation.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 11-12, 20, 23-37, 39-64 and 71-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glen et al US 4,452,817 taken with Meadow et al., WO

03/017977 A1 (of record) in view of May et al., US 6,140,374 (of record) and Lee et al., US 6,743,436 B1 (of record).

Glen et al teach the instant claims 1 and 11 an aqueous formulation comprising: a. 2,6-diisopropylphenol 1-2 %, water, (see col. 7 lines 17-24) of said formulation as required claims 1 and 20, water, block-copolymer PLURONIC F68- commonly known as Poloxamer 188 or P188 (10%). A pH modifier citric acid (see col. 3, lines 7-10) as in claim 1 and 32. It is obvious that the solution of example 10 is clear, because where the solution is not clear, the reference teaches how to obtain a clear solution (see example 9, col. 6, lines 6-8). Absent factual evidence, a clear solution is taught.

Glen also teaches the concentration of 2,6-diisopropylphenol ranges from 0.5-5% as required by claims 20 and 51-57. See col.2, lines 46-48.

With regards to claims 27-28, the PEG is 400 (see col. 2, lines 36-39 and col. 6, lines 29). Glen et al. also teach antimicrobial excipients included in the formulation as sodium metabisulfate (see col. 3, lines 3) as in claims 35-36.

Claims12, 39-57, 66 72 and 75 where the total amount of the block polymer is from 5-10% of said formulation (see col. 3 lines 27-28) an over lap of the range exist, therefore will be obvious to one of ordinary skill to modify to achieve the instantly claimed invention. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the

optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Claims 49-57 requires the PEG to be 10 %(which is included in the range up to 15%), therefore the claim limitations are met (see col. 3 lines 30-31). Glen teaches as required by current claims 32, 49, 58, 67, citric acid in the composition (see col. 3 lines 10-13).

Glen also teaches the formulation is administered to a mammal (see col.1 lines 7-8) to induce anesthesia recited in claim 73. Claim 74 is obvious, as the formulation is in a container because in other to dispense the formulation would have to be in a container. With regard to the different percentages as required by instant claims 29-31, see In re Aller explained above.

Glen et al. did not state the concentration of the citric acid as disclosed in the instant application, the use of citric aid is to maintain the pH of the composition, therefore one of ordinary skill in the art will modify the concentration of the acid to achieve the desired pH level of the formulation.

As to claim 49, 66 and 72, Lee teaches the block copolymer is less that 10 % (see cols. 7 and 8).

Lee et al. teach an anesthetic composition of 2,6-diisopropylphenol solution comprising a poloxamer 188 in an amount of 8% (see col. 7 line 32+) in claims 51, 52, 56, and 7% as recited in claims 53-54 and 57 (see 6 line 65+). Also the reference teaches the range of PEG from 0.5-5% (see col.7 lines 16-65) as recited in claims 39-57. The Lee et al. reference teach the formulation contains polysorbate (see col. 7 lines

47-50) as required in claim 62 containing 2 % polyoxyethylene 20 sorbitan (see col. 7 lines 47-50) in claim 63.

May et al. teach current claims 60-61, 66 and 68 a pharmaceutical formulation containing an antimicrobial agent –benzyl alcohol (see abstract). As to claim 49, 2,6-diisopropylphenol is recited as 1 and 2% w/v of said formulation (see col. 2 line 14) and 1% by w/v (see col. 2 line 16) as in claims 40-48, 51-55.

Also the combine above reference teaches a wide concentration range for copolymers, PEG, citric acid. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a sterile composition consisting of 2,6-diisopropylphenol, poloxamer 188, PEG, water, modify the ranges of the excipient, add an antibacterial agent for the administration to a mammal because, the combined references teach, an anesthetic solution comprising various concentration. One of ordinary skill in the art would have been motivated to optimize the concentration of the surfactants as taught by Lee. Lee et al, however provided motivation to optimize the ranges of surfactants used with the lipid, based upon the examples given (see col. 6), where 4 grams of the surfactant and 0.5 g of PEG versus, 8 grams surfactant and 5 grams PEG, indicating concentration ranges can be optimized, based, upon the lipid use as soluble lipid-soluble drugs are generally poorly soluble in water and possesses limitation as disclosed by Lee et al. (col. 1 lines 64+). Lee further explained (see col. 5. line 4+), the effect of selecting a suitable surfactant to increase the surface tension.

One of ordinary skill in the art would have been motivated to combine the

teaching of Glen et al. with that of Meadow et al. May et al. and Lee et al. to obtain the concentrations as required by the claimed invention and expect a successful results in administering the formulation as an anesthetic to patients. One of the ordinary skills in the art would have known administering anesthesia to patients would vary based on the tolerance, and the condition of the patient in need thereof. It would have been obvious to one of ordinary skill in the ad to add an antimicrobial to the solution to prevent microbial growth in compositions intended for human and/or veterinary use. Therefore the skilled artisan would have incorporated an anti bacterial agent to the formulation. One of ordinary skill in the art would have expected successful results and would have been motivated combining the teachings of the above cited references as the art recognizes the claimed formulation (claim 49) for use as an anesthesia.

Lastly, it would have been obvious to one of ordinary skill in the art to use a purified poloxamer, since the formulation is intended for human.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

Claims 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glen et al US 4,452,817 in view of Meadow et al., WO 03/017977 A1 as applied to claims 49-64, 66-68 and 71-74 above, and further in view of May et al., US 6,140,374 and Lee et al., US 6,743,436 B1.

For the same reasons given above, the use of sodium or potassium hydroxide and hydrochloric acid are well known in the art for modifying pH. One of ordinary skill would have employed any of the pH modifiers to adjust the pH of the solution, use the

base to titrate for pH ranges in the basic range or the hydrochloric acid to adjust in the acidic range.

As to the average particle size of about 30 nanometers, one of ordinary skill in the art would expect the solution having the same ingredients in the same weight percent to have the same characteristics.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ardin H. Marschel 9/2/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

SVG
10/14/06